

## AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

### 1. Paragraph on page 2 starting at line 6 and ending at line 21

Although there has been a significant improvement in the discovery of new catalysts using combinatorial catalysis techniques, many of the techniques relied upon to assay these potential catalysts are still laborious and time consuming. For example, most of the assays rely on the use of traditional gas chromatography or mass spectrometry methods to analyze reaction products and typically can only analyze one sample every few minutes, and additionally require additional time between samples. One example of the progress towards the development of high-throughput screening techniques includes the use of mass tagged chiral acylating agents to diastereoselectively derivatize and automate qualitative electrospray ionization mass spectrometry (ESI-MS) (Guo *et al. Angew. Chem. Int. Ed. Engl.* **1999**, 38, 1755). This method, however, is still laborious and time consuming, particularly for the screening of as many as, or more than, 10,000 products, because each sample must be injected into the mass spectrometer (only samples with differing molecular weights may be combined) and requires approximately two minutes to complete. Therefore, the analysis of 10,000 reaction products, at two minutes per sample, including a 20 minute wash after every 36 samples, would require approximately 17.65 days (working 24 hours a day) to complete.

### 2. Paragraph on page 5 starting at line 20 and ending at line 25

In certain embodiments, for each of said chiral detecting reagents, R<sub>1</sub> and R<sub>2</sub> and R<sub>3</sub> and R<sub>4</sub> taken together each comprise a benzene moiety, C<sub>6</sub>H<sub>6</sub>; wherein each of ~~X and Y~~ Z and Y are -C(CH<sub>3</sub>)<sub>2</sub> wherein the linker moiety, L, comprises -(CH)<sub>p</sub>-(CO)-; wherein p is 1-5, and in certain embodiments is 4, and wherein the chiral reagent (CR) comprises a chiral acylating agent having the general structure: -(NH)-(CHR<sub>x</sub>)-COOH, where R<sub>x</sub> comprises a chiral amino acid residue.

### 3. Paragraph on page 6 starting at line 15 and ending at line 19

In certain embodiments, R<sub>1</sub> and R<sub>2</sub> and R<sub>3</sub> and R<sub>4</sub> taken together each comprise a benzene

moiety, C<sub>6</sub>H<sub>6</sub> ; wherein each of ~~X and Y~~ Z and Y are -C(CH<sub>3</sub>)<sub>2</sub> ; wherein the linker moiety comprises -(CH)<sub>p</sub>-(CO)-; wherein p is 1-5, and in certain embodiments is 4, and wherein the chiral reagent comprises a chiral acylating agent having the general structure: -(NH)-(CHR<sub>x</sub>)-COOH, where R<sub>x</sub> comprises a chiral amino acid residue.

**4. Paragraph on page 7 starting at line 21 and ending at line 26**

In still other embodiments for the kits as described above and as disclosed herein, R<sub>1</sub> and R<sub>2</sub> and R<sub>3</sub> and R<sub>4</sub> taken together each comprise a benzene moiety, C<sub>6</sub>H<sub>6</sub>; wherein each of ~~X and Y~~ Z and Y are -C(CH<sub>3</sub>)<sub>2</sub> wherein the linker moiety comprises -(CH)<sub>p</sub>-(CO)-; wherein p is 1-5, and in certain embodiments is 4, and wherein the chiral agent comprises a chiral acylating agent having the general structure: -(NH)-(CHR<sub>x</sub>)-COOH, where R<sub>x</sub> comprises a chiral amino acid residue.

**5. Paragraph on page 8 starting at line 26 and ending at line 27**

Figure 7 depicts a scheme for the synthesis of indocarbocyanine and indodicarbocyanine ~~fluorophores~~ fluorophores.

**6. Paragraph on page 8 starting at line 28 and ending at line 29**

Figure 8 depicts the synthesis of Cy3 ~~fluorophore~~ fluorophores conjugates by 'Bu-protected amino acids.

**7. Paragraph starting on page 12 line 30 and ending on page 13 line 7**

The importance of asymmetric synthesis in the chemical and pharmaceutical industry is evidenced by the ever-increasing ~~research~~ research efforts to discover catalysts capable of effecting enantioselective, and even more desirably enantiospecific, transformations (see, for example, Jandeleit *et al.* "Combinatorial Materials Science" *Angew. Chem. Int. Ed.* **1999**, 38, 2494). As mentioned above, despite the increased interest and progress made in new screening methods, one of the biggest obstacles to the discovery of new catalysts, reactions, or reaction conditions is the inability to screen large numbers of products rapidly (for a recent review see,

Reetz, M.T. *Angew. Chem. Int. Ed.* **2001**, *40*, 284-310).

**8. Paragraph on page 15 starting at line 9 and ending at line 27**

In certain other embodiments, the identifier moiety comprises a reagent that is capable of interacting selectively with a particular functional group (and not necessarily with a particular enantiomer) and thus mixtures of reaction components can be contacted with identification reagents comprising a reagent that is capable of interacting selectively with a particular functional group either prior to, simultaneously with, or after contacting with chiral detecting agent. Once the identification moiety interacts selective with a particular functionality (*e.g.*, an amine, or other functional group), the detection reagent enables the unique identification of the functionality of interest. To clarify, it would be possible in certain embodiments to develop an identification reagent (or set of reagents) in which one of the set comprises, for example, an identification moiety capable of interacting selectively with a functional group in the starting materials, and has a unique detection agent (distinct from detection agents used in chiral detection ~~reagents~~ reagents, for example) to enable determination of the amount of starting material present. By combining the information obtained from contacting with a set of chiral detecting regents and contacting with a set (or one) of identification reagents, the percent yield can be determined. Additionally, a set of identification reagents developed for a variety of functional groups and each uniquely identifiable would be useful in the "screening" of novel reactions (where an unexpected functionality is obtained, for example), or for the analysis of reaction progression.

**9. Paragraph on page 16 starting at line 14 and ending at line 27**

It will be appreciated that the method of the present invention can be utilized to evaluate the components (*e.g.*, starting materials and reaction products) from a variety of reactions, and in certain embodiments from a variety of asymmetric reactions. It will be appreciated that a variety of reaction conditions and parameters may be tested and evaluated by analyzing the products of the present invention. For example, certain ~~paramaters~~ parameters which can be investigated and evaluated are the discovery of novel catalysts, the discovery of novel

stoichiometric reagents, the optimization of reaction conditions, and even the discovery of heretofore unknown or ~~unachievable~~ unachievable asymmetric reactions using known catalysts, to name a few. It will be appreciated that the reaction products from any experiment generating reaction products, and in certain embodiments, enantiomeric products, may be analyzed using the method of the present invention. Additionally, as also discussed herein, the method of the invention can be utilized to determine the chemical functionality and thus percent yields of components of a reaction mixture.

**10. Paragraph starting on page 24 at line 18 and ending on page 25 at line 3**

In one embodiment, the method of the present invention utilizes microarrays of reaction products, namely *reaction microarrays*. An advantage of the use of reaction microarrays for catalyst discovery using combinatorial methods is the determination of enantiomeric ratios from every reaction, as opposed to other screens that may identify only a few catalysts that give the highest enantiomeric ratios. A large amount of information can be extracted from each set of experiments relating catalyst structure, additives and conditions to the degree of asymmetric induction and reaction conversion. Encoded within this data are important trends that would not have been uncovered by screens that only identify the most active catalysts. In analogy to the development of bioinformatics resulting from DNA ~~microarrays~~ microarrays, chemical informatics programs will be necessary in order to organize and mine the data returned by reaction microarrays from tens-of-thousands of catalysis experiments or more. Reaction microarrays can also help to accelerate catalysis discovery by lowering the barrier to attempting catalytic enantioselective reactions with new and unorthodox chiral ligand-metal combinations. The information returned by these experiments may lead to a better understanding of the complex chemical forces involved in asymmetric catalysis and the development of novel catalysts.

**11. Paragraph on page 44 starting at line 18 and ending at line 26**

To an oven-dried 50 ml round-bottom flask fitted with a septaed condenser, cooled under an argon atmosphere, and charged with (R)-*tert*-leucine (245.7 mg, 1.87 mmol) and di-*tert*-butyl

dicarbonate (818 mg, 3.75 mmol) was added 3.6 mL anhydrous methanol followed by 400  $\mu$ L of freshly distilled triethylamine. The reaction was heated with stirring to 50  $^{\circ}$ C for 30 minutes after all *tert*-leucine had disappeared. The reaction was concentrated *in vacuo*, 20 mL ice-cold dilute HCl (pH  $\sim$ 2) was added, and the reaction was stirred for 10 minutes. The mixture was immediately extracted three times with ethyl acetate, and the combined organic extracts were dried over ~~anhydrous~~ anhydrous magnesium sulfate, filtered, and concentrated *in vacuo* to afford **24h** as a white solid.

**12. Paragraph on page 45 starting at line 11 and ending at line 20**

To an oven-dried 50 ml round-bottom flask fitted with a septaed condenser, cooled under an argon atmosphere, and charged with (S)-phenylglycine (378 mg, 2.5 mmol) and di-*tert*-butyl dicarbonate (1.09 g, 5.0 mmol) was added 3.5 mL anhydrous methanol followed by 1.5 mL of freshly distilled triethylamine. The reaction was heated with stirring to 50  $^{\circ}$ C for 30 minutes after all *tert*-leucine had disappeared. The reaction was concentrated *in vacuo*, 20 mL ice-cold dilute HCl (pH  $\sim$ 2) was added, and the reaction was stirred for 10 minutes. The mixture was immediately extracted three times with ethyl acetate, and the combined organic extracts were dried over ~~anhydrous~~ anhydrous magnesium sulfate, filtered, and concentrated *in vacuo*. Crystallization from petroleum ether afforded 557 mg (89%) of **24k** as white crystals.

**13. Paragraph on page 61 starting at line 2 and ending at line 5**

In the arrays of the chiral amino acids the enantiomer in excess in columns 1 ~~through~~ through 5 was intended to be D, while the L enantiomer was intended to be the excess enantiomer in columns 7 through 12. Columns 6 and 7 were intended to contain a nearly racemic (0% enantiomeric excess) mixture.

**14. Paragraph starting on page 66 at line 16 and ending on page 67 at line 4**

Individual spots were analyzed using GenePix 4000A software, and the background-subtracted mean of ratios (arithmetic mean of background-subtracted pixel-by-pixel ratios of raw pixel intensities) was used for calculation of kinetic resolution and subsequent calculation of

measured *e.e.* The mean of ratios value for each racemic (0% *e.e.*) chiral amino acid was used to determine the fluorescent intensity normalization factor for all other mean of ratios values for that amino acid. The normalized ratios for enantiopure (>99% *e.e.*) amino acids were applied to a rearranged version of Horeau's equation, where for 100% *e.e.*,  $s = y$ , and a quantitative value for kinetic resolution is obtained directly. This calculated *s* value for each enantiopure amino acid was then used to calculate the *e.e.* for each spot with that enantiomer in excess. Mean of ratios data was rejected from further consideration if the standard deviation in the mean of ratios exceeded one-half the mean of ratios value. Data from 12 arrays were pooled, and statistical outliers were rejected from pooled statistical analysis using the Q-test at 95% CL. The resulting body of data for each amino acid at each actual *e.e.* was evaluated for: number of valid cases; arithmetic mean; standard error of the mean; variance; standard deviation; minimum value; maximum value; range; median; and geometric mean. The arithmetic mean was plotted against the actual ~~enantiomeric~~ enantiomeric excess (100% *e.e.* D-amino acid arbitrarily defined as +100%; 100% *e.e.* L-amino acid as -100%) with error bars defined by values of the standard error of the mean. Plots, as defined above, were fit to a straight line of form  $y = ax + b$  using non-weighted linear least-squares analysis.